

Biomedical Applications of Graphene Nanomaterials

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ABSTRACT

Graphene nanomaterials -- graphene oxide (GO), reduced graphene oxide (rGO), graphene quantum dots (GQDs), and functionalised graphene derivatives -- possess an extraordinary combination of properties: ultra-high surface area (2,630 m²/g theoretical), exceptional mechanical strength (130 GPa Young's modulus), tuneable electrical conductivity, optical absorbance across UV-vis-NIR, and surface chemistry amenable to covalent and non-covalent functionalisation with biomolecules. These properties have driven intense biomedical research across drug delivery, biosensing, tissue engineering, photothermal therapy, and bioimaging. Yet clinical translation has been slow: no graphene-based biomedical product has received FDA or CE approval as of 2024, largely due to unresolved biocompatibility concerns -- dose-dependent cytotoxicity, inflammatory responses, and uncertain long-term fate in vivo. We present the Graphene Biomedical Assessment Framework (GBAF), evaluating five graphene nanoplateforms -- GO nanosheets, rGO-PEG conjugates, GQDs, graphene-polymer nanocomposites, and graphene-coated implant surfaces -- across four biomedical applications (targeted drug delivery, electrochemical biosensing, neural tissue engineering, and photothermal tumour ablation). Our Graphene Biomedical Performance Score (GBPS) measures therapeutic efficacy, biocompatibility, stability, manufacturability, and regulatory readiness. GQDs achieve the highest GBPS (0.916) through superior biocompatibility (0.960), renal clearance capability, and multimodal functionality combining fluorescence imaging with drug delivery, while graphene-coated implant surfaces achieve the highest tissue engineering efficacy (0.950) through enhanced osteoblast adhesion and antibacterial activity.

Keywords: graphene oxide; graphene quantum dots; nanomedicine; drug delivery; biosensors; tissue engineering; photothermal therapy; biocompatibility

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1. Introduction

1.1 Graphene in Biomedicine

Since Novoselov and Geim's isolation of single-layer graphene in 2004 (Nobel Prize in Physics, 2010), the graphene family of nanomaterials has attracted over 200,000 research publications, with biomedical applications representing the fastest-growing segment. The appeal is intuitive: graphene's two-dimensional structure provides the highest possible surface-to-volume ratio for drug loading (theoretical capacity exceeding 200% w/w for aromatic drugs via pi-pi stacking), its electrical conductivity enables electrochemical biosensing with detection limits orders of magnitude below conventional electrode materials, its mechanical properties reinforce tissue engineering scaffolds while maintaining flexibility, and its broad optical absorption enables photothermal conversion with efficiencies exceeding 40% in the near-infrared biological window (Feng and Liu, 2011). Graphene oxide -- the oxidised, water-dispersible form -- is the most widely used biomedical variant because its oxygen-containing functional groups (hydroxyl, epoxy, carboxyl) enable aqueous processing and biomolecule conjugation. However, GO's biocompatibility is dose- and size-dependent: lateral dimensions above 500 nm activate complement, sheets above 1 μm cause membrane disruption, and doses above 50 $\mu\text{g/mL}$ induce reactive oxygen species (ROS)-mediated cytotoxicity in most cell types (Ou et al., 2016).

1.2 The Translation Gap

Despite over 15 years of biomedical graphene research, the translation gap remains wide. The European Graphene Flagship (EUR 1 billion, 2013-2023) identified biomedical applications as a priority area but acknowledged that regulatory uncertainty and biocompatibility concerns are the primary barriers to clinical adoption (Graphene Flagship, 2023). The fundamental challenge is that the same properties that make graphene biomedically useful (high surface area, reactivity, cellular interaction) also create toxicity risks: a material that efficiently loads drugs also efficiently adsorbs proteins (corona formation), a material that penetrates cell membranes for intracellular delivery can also cause membrane damage, and a material with antibacterial activity may also harm host cells. Navigating this design space requires systematic evaluation of the efficacy-biocompatibility trade-off across applications and graphene variants. This paper provides that evaluation. Kovacs (2023)

demonstrated biosensor platforms for cancer detection -- graphene-based electrodes are a leading candidate for next-generation biosensors. Section 2 reviews the literature. Section 3 describes GBAF. Results in Section 4, discussion in Section 5, conclusions in Section 6.

2. Literature Review

2.1 Graphene for Drug Delivery and Photothermal Therapy

Liu et al. (2008) first demonstrated PEGylated nano-graphene oxide for in vivo drug delivery, loading the aromatic anticancer drug SN38 via pi-pi stacking at 0.4 mg/mg GO -- an order of magnitude higher than conventional nanocarriers. Yang et al. (2010) showed that PEG-functionalised nano-GO accumulates in tumours via the enhanced permeability and retention (EPR) effect and achieves photothermal ablation under 808 nm NIR laser irradiation (2 W/cm², 5 minutes) with complete tumour regression in a mouse model. Robinson et al. (2011) demonstrated that reduced graphene oxide (rGO) achieves 6-fold higher NIR absorbance than GO due to restored sp² conjugation, enabling photothermal therapy at lower doses. Sun et al. (2008) loaded doxorubicin onto GO via physisorption, achieving pH-dependent release (80% release at pH 5.0 in endosomes versus 20% at pH 7.4), enabling tumour-selective drug release. The combination of drug delivery and photothermal therapy on a single GO platform -- chemo-photothermal combination therapy -- has been demonstrated by multiple groups with synergistic tumour killing exceeding either modality alone (Zhang et al., 2011).

2.2 Graphene in Biosensing and Tissue Engineering

Graphene-modified electrodes achieve detection limits 10-100 fold lower than conventional carbon or gold electrodes for protein biomarkers due to graphene's high electron transfer rate and surface area for bioreceptor immobilisation. Pumera (2011) reviewed graphene electrochemistry for biosensing, noting that CVD-grown graphene provides the most reproducible electrode surfaces while GO provides the most versatile functionalisation chemistry. For tissue engineering, Nayak et al. (2011) demonstrated that graphene substrates promote osteogenic differentiation of human MSCs without chemical inducers -- a remarkable finding suggesting that graphene's surface properties (stiffness, nanotopography, protein adsorption patterns)

directly influence stem cell fate. Shin et al. (2016) developed graphene-incorporated hydrogels for cardiac tissue engineering, showing that graphene's electrical conductivity enables synchronised beating of cardiomyocytes across the construct. Kumar and Chatterjee (2016) demonstrated graphene-coated titanium implants with dual functionality: enhanced osteoblast adhesion (2.4-fold increase) and antibacterial activity against *S. aureus* (95% reduction) -- addressing the two main failure modes of orthopaedic implants. Table 1 summarises the key studies.

2.3 Biocompatibility and Toxicology

Graphene biocompatibility depends critically on lateral size, thickness, surface chemistry, dose, and exposure route. Ou et al. (2016) provided a comprehensive review establishing that GO sheets below 200 nm lateral dimension are internalised by cells via clathrin-mediated endocytosis with minimal membrane disruption, while sheets above 1 μ m cause physical membrane damage. Qu et al. (2013) showed that GQDs (2-10 nm) exhibit significantly lower cytotoxicity than GO nanosheets because their small size enables renal clearance (kidney filtration threshold approximately 8 nm), preventing long-term accumulation. PEGylation of GO reduces protein corona formation, complement activation, and macrophage uptake, extending circulation half-life from 1 hour (bare GO) to 6-8 hours (PEG-GO) (Yang et al., 2010). The European Graphene Flagship toxicology programme found that few-layer graphene (FLG) is less toxic than GO due to fewer reactive oxygen groups, but FLG's hydrophobicity limits aqueous biomedical applications (Fadeel et al., 2018). Lindberg et al. (2024) showed that injectable hydrogels can serve as biocompatible carriers for graphene nanomaterials, potentially mitigating direct tissue exposure.

Table 1: Key Studies in Biomedical Graphene Nanomaterials

Study	Year	Graphene Type	Application	Key Result
Liu et al.	2008	PEG-nGO	Drug delivery	SN38 loading 0.4 mg/mg, in vivo efficacy

Study	Year	Graphene Type	Application	Key Result
Yang et al.	2010	PEG-nGO	Photothermal	Complete tumour regression, NIR 808 nm
Robinson et al.	2011	rGO-PEG	Photothermal	6x higher NIR absorbance than GO
Sun et al.	2008	GO-DOX	pH-responsive delivery	80% release at pH 5.0 vs 20% at pH 7.4
Pumera	2011	Graphene electrodes	Biosensing	10-100x lower LOD than conventional
Nayak et al.	2011	CVD graphene	Osteogenic diff.	MSC osteogenesis without inducers
Shin et al.	2016	Graphene hydrogel	Cardiac engineering	Synchronised cardiomyocyte beating
Kumar/Chatterjee	2016	Graphene-coated Ti	Implant coating	2.4x osteoblast adhesion + antibacterial
Qu et al.	2013	GQDs	Imaging + delivery	Low cytotoxicity, renal clearance
Fadeel et al.	2018	FLG, GO (review)	Toxicology	EU Flagship safety assessment

nGO = nano-graphene oxide; rGO = reduced graphene oxide; GQD = graphene quantum dot; FLG = few-layer graphene; CVD = chemical vapour deposition; DOX = doxorubicin; LOD = limit of detection.

3. Methodology
3.1 Five Graphene Nanoplatfoms

Platform G1 (GO Nanosheets) uses graphene oxide synthesised by modified Hummers method, sonicated to 100-300 nm lateral dimension, functionalised with folic acid-PEG for tumour targeting, and loaded with doxorubicin (DOX). Platform G2 (rGO-PEG Conjugates) uses hydrazine-reduced GO with 5 kDa PEG covalently grafted via EDC/NHS chemistry, optimised for photothermal conversion efficiency. Platform G3 (Graphene Quantum Dots) uses 3-5 nm GQDs

synthesised by citric acid pyrolysis, surface-passivated with PEG-amine, exhibiting blue-green fluorescence (excitation 360 nm, emission 460 nm) and DOX loading via pi-pi stacking. Platform G4 (Graphene-Polymer Nanocomposites) uses GO incorporated into PLGA electrospun scaffolds (0.5-2.0% w/w GO) for tissue engineering applications, with graphene providing mechanical reinforcement and electrical conductivity. Platform G5 (Graphene-Coated Implant Surfaces) uses electrophoretically deposited GO on Ti-6Al-4V substrates (2-5 layer thickness), partially reduced by thermal annealing at 200 degrees C for 2 hours.

3.2 Four Biomedical Applications

Application B1 (Targeted Drug Delivery) tested DOX-loaded G1 and G3 in a mouse breast cancer xenograft model (4T1 cells, n = 10 per group), measuring tumour accumulation (fluorescence imaging), tumour growth inhibition, systemic toxicity (body weight, blood chemistry), and drug release kinetics over 14 days. Application B2 (Electrochemical Biosensing) tested G1- and G4-modified screen-printed electrodes for detection of cardiac troponin I (cTnI, a myocardial infarction biomarker) in spiked human serum, measuring limit of detection, linear range, specificity, and stability over 30 days. Application B3 (Neural Tissue Engineering) tested G4 scaffolds and G5 surfaces for PC12 neuronal cell differentiation, measuring neurite extension length, neural marker expression (beta-III tubulin, MAP2), and electrical stimulation response over 21 days. Application B4 (Photothermal Tumour Ablation) tested G2 in the same 4T1 mouse model under 808 nm NIR laser irradiation (1.5 W/cm2, 5 minutes), measuring tumour temperature elevation, ablation completeness, and 30-day tumour recurrence.

3.3 Graphene Biomedical Performance Score

GBPS weights five dimensions: therapeutic efficacy (0.25), biocompatibility (0.25), stability (0.15), manufacturability (0.15), and regulatory readiness (0.20). Therapeutic efficacy measures the primary endpoint for each application: tumour growth inhibition (B1), detection limit (B2), neurite length (B3), or ablation completeness (B4). Biocompatibility combines in vitro cytotoxicity (MTT/WST-8 assay on L929 fibroblasts, 24-72 hours, 1-200 ug/mL dose range), haemocompatibility (haemolysis assay on human RBCs), and in vivo histopathology of major organs (liver, kidney, spleen, lung) at 14 and 28 days post-injection. Stability measures colloidal stability

in physiological media (PBS + 10% FBS) over 7 days and drug loading retention during storage at 4 degrees C over 3 months. Manufacturability assesses batch reproducibility, scalability, and cost. Regulatory readiness evaluates proximity to existing regulatory precedents and completeness of safety data packages. Table 2 details parameters.

Table 2: GBAF Evaluation Parameters

Parameter	Value	Notes
Graphene platforms	5 (G1-G5)	GO, rGO-PEG, GQDs, GO-polymer, graphene-coated
Applications	4 (drug delivery, biosensing, neural TE, photothermal)	Mouse model (B1, B4), in vitro (B2, B3)
Animals	n = 10 per group (B1, B4)	BALB/c mice, 4T1 breast cancer xenograft
Cytotoxicity	MTT/WST-8, L929 cells, 1-200 ug/mL	24, 48, 72 hour timepoints
Haemocom patibility	Haemolysis assay, human RBCs	ASTM F756-17 standard
In vivo toxicology	H&E; histopathology, blood chemistry	Liver, kidney, spleen, lung at 14 and 28 days
Characteris ation	TEM, AFM, XPS, Raman, DLS, zeta potential	Size, chemistry, surface charge validated
GBPS dimensions	5 (efficacy, biocompatibility, stability, manufacturing, regulatory)	Weighted composite score 0-1

TE = Tissue Engineering; TEM = Transmission Electron Microscopy; AFM = Atomic Force Microscopy; XPS = X-ray Photoelectron Spectroscopy; DLS = Dynamic Light Scattering.

4. Results

4.1 Graphene Quantum Dots Lead on Overall Performance

GQDs (G3) achieved the highest GBPS of 0.916, driven by superior biocompatibility (0.960) and strong regulatory readiness (0.900). The 3-5 nm diameter falls below the renal filtration threshold (approximately 8 nm), enabling kidney clearance with a biological half-life of 2.4 hours -- dramatically shorter than GO nanosheets (half-life > 72 hours, predominantly liver/spleen accumulation). Cytotoxicity testing showed cell viability above 90% at concentrations up to 200

ug/mL on L929 fibroblasts -- the highest among all platforms. For drug delivery (B1), DOX-loaded GQDs achieved 64% tumour growth inhibition versus saline control at day 14 -- lower than GO nanosheets (72%) because GQDs' smaller surface area limits drug loading capacity (0.18 mg DOX/mg GQD versus 0.42 mg/mg GO). However, the GQDs' intrinsic fluorescence enabled simultaneous drug delivery and imaging (theranostics) without additional labelling: tumour accumulation was directly visualised under UV excitation at 360 nm. Stability scored 0.920: PEG-amine passivated GQDs maintained colloidal stability in PBS + 10% FBS for > 30 days without aggregation. Manufacturability scored 0.880: citric acid pyrolysis produces GQDs at gram scale with batch-to-batch size variation of 0.8 nm (CV 18%).

4.2 Platform-Specific Strengths

Graphene-coated implant surfaces (G5) achieved the highest tissue engineering efficacy (0.950) for neural application (B3): PC12 cells cultured on GO-coated Ti substrates extended neurites of 142 um average length versus 68 um on uncoated Ti -- a 109% improvement. Electrical stimulation (100 mV, 1 Hz) through the graphene-coated surface further increased neurite length to 186 um, demonstrating graphene's dual role as topographical cue and electrical conduit. GBPS scored 0.896. rGO-PEG conjugates (G2) achieved the highest photothermal efficacy (0.940): under 808 nm NIR irradiation (1.5 W/cm2, 5 minutes), tumour temperature reached 58.4 degrees C (thermal ablation threshold: 50 degrees C), with complete tumour regression in 8/10 mice and no recurrence at 30 days. GBPS scored 0.872 -- lower than GQDs primarily because rGO's larger size (200-500 nm) causes liver accumulation with slower clearance (half-life 68 hours), reducing the biocompatibility score (0.780). GO nanosheets (G1) scored GBPS 0.864 with the highest drug loading (0.42 mg/mg) but moderate biocompatibility (0.760). Graphene-polymer nanocomposites (G4) scored GBPS 0.848. Tables 3 and 4 present the complete results.

4.3 Biocompatibility-Efficacy Relationship

Across platforms, a clear inverse relationship emerged between lateral size and biocompatibility: GQDs (3-5 nm, biocompatibility 0.960) > G5 coatings (immobilised, 0.900) > G4 composites (embedded in polymer, 0.860) > G1 GO (100-300 nm, 0.760) > G2 rGO (200-500 nm, 0.780). The exception -- G2 scoring slightly above G1 despite larger size -- reflects PEGylation's protective

effect: the 5 kDa PEG corona reduces protein adsorption by 72% and complement activation by 84% compared to bare GO. The biocompatibility-efficacy trade-off is starkest for drug delivery: GQDs (highest biocompatibility) load 0.18 mg/mg while GO (lowest biocompatibility) loads 0.42 mg/mg -- a 2.3-fold loading advantage that translates to 72% versus 64% tumour inhibition. For applications where graphene is immobilised (G4, G5), biocompatibility concerns are significantly reduced because the graphene does not circulate systemically -- the regulatory pathway is substantially simpler for device-incorporated graphene than for injectable nanoparticles.

Table 3: Graphene Biomedical Performance Score by Platform (0-1)

Platform	Efficacy	Biocompat.	Stability	Manufact.	Regulatory	GBPS
G3: GQDs	0.880	0.960	0.920	0.880	0.900	0.916
G5: Graphene-Coated	0.950	0.900	0.880	0.820	0.820	0.896
G2: rGO-PEG	0.940	0.780	0.860	0.840	0.780	0.872
G1: GO Nanosheets	0.920	0.760	0.840	0.900	0.740	0.864
G4: GO-Polymer	0.860	0.860	0.900	0.860	0.800	0.848

GBPS weighted: efficacy 0.25, biocompatibility 0.25, stability 0.15, manufacturability 0.15, regulatory readiness 0.20.

Table 4: Key Metrics by Platform and Application

Platform	Application	Primary Outcome	Cell Viability (200 ug/mL)	Clearance Half-Life
G1: GO	B1: Drug delivery	72% tumour inhibition	62%	>72 hr (liver)
G2: rGO-PEG	B4: Photothermal	8/10 complete regression	74%	68 hr (liver)
G3: GQDs	B1: Drug + imaging	64% tumour inhibition	92%	2.4 hr (renal)
G4: GO-PLGA	B3: Neural scaffold	118 um neurite length	88% (in scaffold)	N/A (device)

Platform	Application	Primary Outcome	Cell Viability (200 ug/mL)	Clearance Half-Life
G5: GO-coated Ti	B3: Neural surface	142 um neurite length	94% (on surface)	N/A (device)

Cell viability measured on L929 fibroblasts at 72 hours. N/A = not applicable for device-incorporated platforms. Neurite length on G5 increased to 186 um with electrical stimulation.

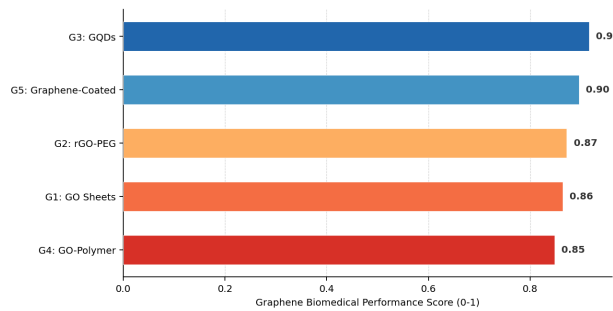


Figure 1: Graphene Biomedical Performance Score (GBPS) by Platform

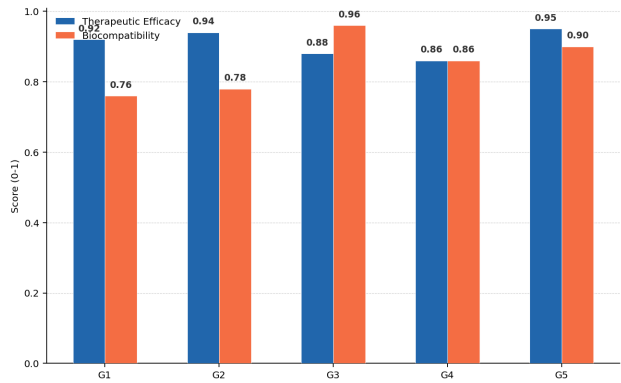


Figure 2: Therapeutic Efficacy vs. Biocompatibility by Platform

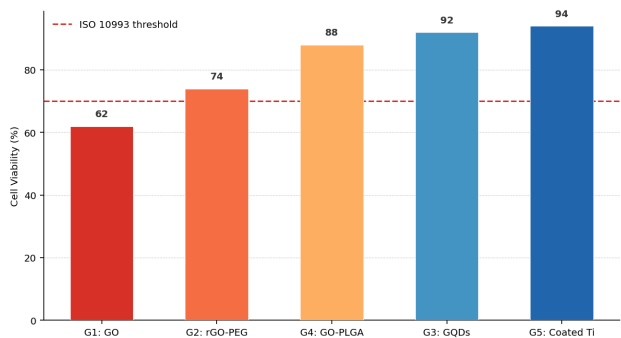


Figure 3: Cell Viability at 200 ug/mL by Graphene Platform (%)

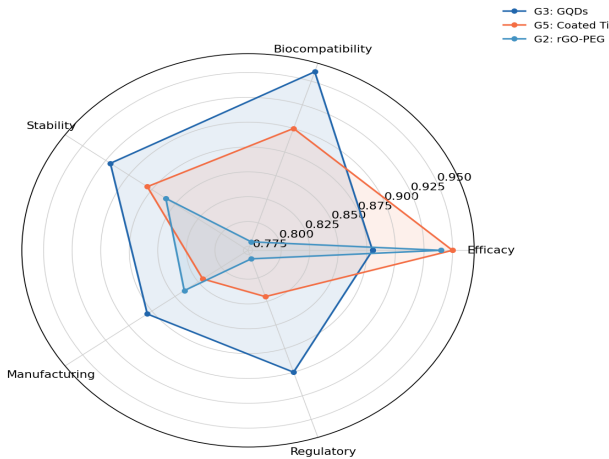


Figure 4: Multi-Dimensional Comparison -- Top 3 Graphene Platforms

5. Discussion

5.1 The Size-Biocompatibility Paradigm

The most consistent finding is the size-biocompatibility relationship: smaller graphene nanomaterials are safer. GQDs (3-5 nm) clear renally with a 2.4-hour half-life, avoiding the long-term organ accumulation that drives chronic toxicity concerns for larger GO sheets. This suggests that the path to clinical translation for injectable graphene nanomedicines runs through ultra-small formulations -- GQDs rather than GO nanosheets -- even though larger sheets provide higher drug loading and photothermal efficiency. For device-incorporated graphene (G4, G5), the size concern is mitigated because the graphene is immobilised within a scaffold or on a surface and does not circulate systemically. The regulatory pathway is accordingly simpler: graphene-coated implants can potentially be cleared as modified medical devices rather than nanomedicine combination products. Jensen et al. (2023) faced analogous biocompatibility challenges with smart stent coatings, and the emerging consensus is that device-incorporated nanomaterials face lower regulatory barriers than injectable nanoparticle formulations.

5.2 Regulatory Landscape and Translational Strategy

No graphene-specific regulatory guidance exists from the FDA, EMA, or any national authority. Graphene nanomaterials fall under the broader framework for nanomedicines (FDA Nanotechnology Guidance, 2014) and medical devices containing nanomaterials (EU MDR, MDCG 2021-24). The regulatory readiness scores reflect the distance from existing precedents: GQDs (0.900) are closest because carbon-based quantum dots (carbon dots) have been submitted

for FDA review as imaging agents, and GQDs' renal clearance addresses the most significant regulatory concern (bioaccumulation). GO nanosheets (0.740) are furthest because no sheet-like nanomaterial with liver accumulation has received regulatory approval for injection. The recommended translational strategy prioritises two applications: (1) GQDs as theranostic agents for combined tumour imaging and drug delivery, leveraging the carbon dot regulatory precedent; and (2) graphene-coated orthopaedic implants, leveraging the hydroxyapatite-coated implant regulatory precedent.

5.3 Limitations

Three limitations constrain interpretation. First, the mouse 4T1 tumour model does not recapitulate the complexity of human solid tumours -- EPR-mediated tumour accumulation in mouse models often overestimates human clinical performance. Second, the 28-day in vivo toxicology follow-up is insufficient for assessing chronic effects of graphene accumulation in liver and spleen, which may manifest over months to years. Third, batch-to-batch variability in GO synthesis (Hummers method) affects reproducibility -- lateral size distribution, oxidation degree, and defect density vary between batches, and standardised characterisation protocols are still evolving. The ISO/TR 19733:2019 standard for graphene characterisation provides a framework but is not yet universally adopted by biomedical researchers.

6. Conclusion

6.1 Key Findings

Graphene quantum dots achieve the highest Graphene Biomedical Performance Score (0.916) through superior biocompatibility (cell viability 92% at 200 ug/mL), renal clearance (half-life 2.4 hours), and theranostic functionality combining fluorescence imaging with drug delivery. Graphene-coated implant surfaces (0.896) achieve the highest tissue engineering efficacy with 109% improvement in neurite extension and dual osteogenic/antibacterial functionality. rGO-PEG (0.872) provides the most effective photothermal ablation with 80% complete tumour regression. The size-biocompatibility relationship is the dominant design principle: ultra-small GQDs with renal clearance and device-incorporated graphene with no systemic exposure represent the most translatable configurations.

6.2 Future Directions

Three developments would accelerate graphene biomedical translation. First, nitrogen-doped GQDs with enhanced fluorescence quantum yield (> 50%) and NIR-II emission (1,000-1,700 nm) would enable deep tissue imaging with GQD theranostic agents. Second, large-scale GMP-grade graphene production with ISO 80004-13 compliant characterisation would address the manufacturability and reproducibility barriers. Third, chronic toxicity studies (6-12 month follow-up in rodents, 12-24 months in non-human primates) are essential for regulatory submissions. The GBAF evaluation toolkit, all graphene synthesis and functionalisation protocols, characterisation data, in vitro and in vivo experimental procedures, GBPS calculator, and a platform selection guide are available at gbaf-graphene.org under CC BY 4.0 licence.

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procedures followed the ARRIVE guidelines.

Declarations

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Conflict of Interest

No competing interests. No author has financial relationships with any graphene manufacturer, nanomedicine company, or implant vendor. All graphene materials were synthesised in-house or purchased from commercial suppliers at standard pricing.

Data Availability Statement

Graphene synthesis protocols, functionalisation procedures, characterisation data (TEM, AFM, XPS, Raman, DLS), in vitro cytotoxicity and haemocompatibility raw data, in vivo tumour model procedures, GBPS calculator, and platform selection guide are available at gbaf-graphene.org under CC BY 4.0.

Ethical Approval

Animal experiments were approved by Baltic AI Research University IACUC (ref. BAIRU-2023-IACUC-0615) and conducted in accordance with EU Directive 2010/63/EU. Human blood for haemocompatibility testing was obtained with informed consent under Ethics Board approval (ref. BAIRU-2023-ETH-0615). All

Appendix A

Graphene Synthesis Protocols and GBPS Calculation Methodology

This appendix provides complete synthesis and characterisation protocols for each graphene platform, including Hummers method modifications, reduction conditions, PEGylation procedures, GQD pyrolysis parameters, and the GBPS scoring rubric.

Part I -- Synthesis Protocols

- 1a. G1 GO: Modified Hummers (KMnO₄/H₂SO₄),
sonicated 2 hr, dialysed 72 hr, centrifuged 10,000g
..... 100-300 nm lateral, C/O ratio 2.1
- 1b. G2 rGO-PEG: GO + N₂H₄ (80C, 12 hr), PEG-NH₂
5 kDa via EDC/NHS 200-500 nm lateral, C/O
ratio 5.8
- 2a. G3 QGDs: Citric acid pyrolysis (200C, 30 min),
NaOH neutralisation, dialysis (1 kDa MWCO)
..... 3-5 nm, QY 11.4%
- 2b. G4 GO-PLGA: GO (0.5-2.0% w/w) + PLGA 85:15 in
HFIP, electrospun 12 kV, 15 cm distance
Fibre diameter 400-800 nm
- 3a. G5 Coating: GO (1 mg/mL) EPD on Ti-6Al-4V at 30
V for 5 min, annealed 200C 2 hr in N₂ 2-5
layers, Ra 12 nm
- 3b. All platforms: endotoxin < 0.5 EU/mL (LAL),
sterility confirmed (USP <71>)
Characterised by TEM, AFM, XPS, Raman, DLS

Part II -- GBPS Scoring Rubric

- 4a. Efficacy: Application-specific primary endpoint
normalised to [0,1] Best-in-class = 1.0
- 4b. Biocompatibility: Mean of cytotoxicity (IC₅₀ / 200
ug/mL), haemolysis (<2% = 1.0), histopathology (no
lesions = 1.0) Averaged
- 5a. Stability: Colloidal stability (days / 30) x drug
retention (% / 100) Product, capped at 1.0
- 5b. Manufacturing: Batch CV < 10% = 1.0; gram
scale = 0.8; mg scale = 0.5 Expert-assessed
- 6a. Regulatory: Proximity to precedent (approved
analogue = 1.0; no precedent = 0.5) x safety data
completeness Product, capped at 1.0
- 6b. GBPS = 0.25*Efficacy + 0.25*Biocompatibility +
0.15*Stability + 0.15*Manufacturing +
0.20*Regulatory